AMENDMENT TO THE CLAIMS

The present document amends claims 1, 14, 18, 23, 94, 96-99 and 107, cancels claims 2-13, 15-17, 19, 102, 105, 111, 115, 116, 120 and 121, and add claims 123-149. According to 37 C.F.R. § 1.121(c), after entry of the present amendment, the status of the claims in the case is as follows:

1. (Currently Amended) A composition comprising a first purified antibody, or antigen-binding fragment thereof, and at least a second therapeutic agent; wherein said first antibody ~~binds to phosphatidylserine and has~~ or antigen-binding fragment thereof comprises at least two variable regions that each comprises three CDRs, wherein at least one of said variable regions is:

(a) ~~substantially the same phospholipid binding profile as the monoclonal antibody 3G4 (ATCC PTA 4545); wherein the phospholipid binding profile of the monoclonal antibody 3G4 (ATCC PTA 4545), as determined by relative strength of reactivity in an ELISA, is PS=PA=PI=PG=CL>>PE, wherein > indicates at least 2-fold difference in phospholipid binding and >> indicates at least 10-fold difference in phospholipid binding, each at identical antibody concentrations~~ a heavy chain variable region that comprises variable heavy (VH) CDR1, VH CDR2 and VH CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said VH CDR1 has the amino acid sequence of SEQ ID NO:10, said VH CDR2 has the amino acid sequence of SEQ ID NO:11 and said VH CDR3 has the amino acid sequence of SEQ ID NO:12; or

(b) ~~an affinity for phosphatidylserine of at least equal to the affinity of the monoclonal antibody 3G4 (ATCC PTA 4545) for phosphatidylserine; wherein the~~

~~affinity of the monoclonal antibody 3G4 (ATCC PTA 4545) for phosphatidylserine, as determined in said ELISA, has an EC_{50} value of 0.040 μg/ml;~~ a light chain variable region that comprises a variable light (VL) CDR1, VL CDR2 and VL CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said VL CDR1 has the amino acid sequence of SEQ ID NO:13, said VL CDR2 has the amino acid sequence of SEQ ID NO:14 and said VL CDR3 has the amino acid sequence of SEQ ID NO:15 ~~and wherein said ELISA comprises:~~

~~(i) adding phosphatidylserine to a solid support;~~

~~(ii) blocking with a blocking buffer comprising 10% serum;~~

~~(iii) adding a primary antibody diluted in said blocking buffer, wherein said primary antibody is said antibody or antigen binding fragment thereof, that binds to phosphatidylserine; and~~

~~(iv) detecting bound primary antibody using a secondary antibody that binds to said primary antibody~~.

Claims 2-13 canceled

14. (Currently Amended) The composition of claim 1, wherein said first antibody is an antigen-binding fragment of an antibody.

Claims 15-17 canceled

18. (Currently Amended) The composition of claim ~~17~~ 14, wherein said first antibody comprises ~~an~~ said antigen-binding ~~region~~ fragment of said antibody operatively attached to a human antibody ~~framework or~~ constant region.

Claims 19-22 canceled

23. (Currently Amended) The composition of claim 1, wherein said first antibody is prepared by a process comprising immunizing an animal with activated endothelial cells and selecting from the immunized animal an antibody as defined in claim 1.

Claims 24-50 canceled

51. (Previously Presented) The composition of claim 1, wherein said composition is a pharmaceutically acceptable composition.

52. (Original) The composition of claim 51, wherein said pharmaceutically acceptable composition is formulated for parenteral administration.

Claims 53-93 canceled

94. (Currently Amended) A composition comprising a first purified antibody ~~that binds to phosphatidylserine and has~~ and at least a second therapeutic agent; wherein said first antibody

comprises at least two variable regions that each comprises three CDRs, wherein at least one of said variable regions is:

(a) ~~substantially the same phospholipid binding profile as the monoclonal antibody 3G4 (ATCC PTA 4545); wherein the phospholipid binding profile of the monoclonal antibody 3G4 (ATCC PTA 4545), as determined by relative strength of reactivity in an ELISA, is PS=PA=PI=PG=CL>>PE, wherein > indicates at least 2-fold difference in phospholipid binding and >> indicates at least 10-fold difference in phospholipid binding, each at identical antibody concentrations~~ a heavy chain variable region that comprises variable heavy (VH) CDR1, VH CDR2 and VH CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said VH CDR1 has the amino acid sequence of SEQ ID NO:10, said VH CDR2 has the amino acid sequence of SEQ ID NO:11 and said VH CDR3 has the amino acid sequence of SEQ ID NO:12; or

(b) ~~an affinity for phosphatidylserine of at least equal to the affinity of the monoclonal antibody 3G4 (ATCC PTA 4545) for phosphatidylserine; wherein the affinity of the monoclonal antibody 3G4 (ATCC PTA 4545) for phosphatidylserine, as determined in said ELISA, has an EC_{50} value of 0.040 μg/ml;~~ a light chain variable region that comprises a variable light (VL) CDR1, VL CDR2 and VL CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said VL CDR1 has the amino acid sequence of SEQ ID NO:13, said VL CDR2 has the amino acid sequence of SEQ ID NO:14 and said VL CDR3 has the amino acid sequence of SEQ ID NO:15

~~and wherein said ELISA comprises:~~

~~(i) adding phosphatidylserine to a solid support;~~

~~(ii) blocking with a blocking buffer comprising 10% serum;~~

~~(iii) adding a primary antibody diluted in said blocking buffer, wherein said primary antibody is said antibody or antigen-binding fragment thereof, that binds to phosphatidylserine; and~~

~~(iv) detecting bound primary antibody using a secondary antibody that binds to said primary antibody~~.

Claim 95 canceled

96. (Currently Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a biologically effective amount of a first purified antibody, or antigen-binding fragment thereof, and at least a second therapeutic agent; wherein said first antibody ~~is an antibody as defined in claim 1~~ or antigen-binding fragment thereof comprises at least two variable regions that each comprises three CDRs, wherein at least one of said variable regions is:

(a) a heavy chain variable region that comprises variable heavy (VH) CDR1, VH CDR2 and VH CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said VH CDR1 has the amino acid sequence of SEQ ID NO:10, said VH CDR2 has the amino acid sequence of SEQ ID NO:11 and said VH CDR3 has the amino acid sequence of SEQ ID NO:12; or

(b) a light chain variable region that comprises a variable light (VL) CDR1, VL CDR2 and VL CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said VL CDR1 has the amino acid

sequence of SEQ ID NO:13, said VL CDR2 has the amino acid sequence of SEQ ID NO:14 and said VL CDR3 has the amino acid sequence of SEQ ID NO:15.

97. (Currently Amended) A kit comprising, in at least a first container, a first purified antibody, or antigen-binding fragment thereof, and at least a second therapeutic agent; wherein said first antibody ~~binds to phosphatidylserine and has~~ or antigen-binding fragment thereof comprises at least two variable regions that each comprises three CDRs, wherein at least one of said variable regions is:

(a) ~~substantially the same phospholipid binding profile as the monoclonal antibody 3G4 (ATCC PTA 4545); wherein the phospholipid binding profile of the monoclonal antibody 3G4 (ATCC PTA 4545), as determined by relative strength of reactivity in an ELISA, is PS=PA=PI=PG=CL>>PE, wherein > indicates at least 2-fold difference in phospholipid binding and >> indicates at least 10-fold difference in phospholipid binding, each at identical antibody concentrations~~ a heavy chain variable region that comprises variable heavy (VH) CDR1, VH CDR2 and VH CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said VH CDR1 has the amino acid sequence of SEQ ID NO:10, said VH CDR2 has the amino acid sequence of SEQ ID NO:11 and said VH CDR3 has the amino acid sequence of SEQ ID NO:12; or

(b) ~~an affinity for phosphatidylserine of at least equal to the affinity of the monoclonal antibody 3G4 (ATCC PTA 4545) for phosphatidylserine; wherein the affinity of the monoclonal antibody 3G4 (ATCC PTA 4545) for phosphatidylserine, as determined in said ELISA, has an EC_{50} value of~~

~~0.040 µg/ml;~~ a light chain variable region that comprises a variable light (VL) CDR1, VL CDR2 and VL CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said VL CDR1 has the amino acid sequence of SEQ ID NO:13, said VL CDR2 has the amino acid sequence of SEQ ID NO:14 and said VL CDR3 has the amino acid sequence of SEQ ID NO:15

~~and wherein said ELISA comprises:~~

~~(i) adding phosphatidylserine to a solid support;~~

~~(ii) blocking with a blocking buffer comprising 10% serum;~~

~~(iii) adding a primary antibody diluted in said blocking buffer, wherein said primary antibody is said antibody or antigen binding fragment thereof, that binds to phosphatidylserine; and~~

~~(iv) detecting bound primary antibody using a secondary antibody that binds to said primary antibody~~.

98. (Currently Amended) A hybridoma that produces a monoclonal antibody that ~~binds to phosphatidylserine and has~~ comprises two variable regions that each comprises three CDRs, wherein at least one of said variable regions is:

(a) ~~substantially the same phospholipid binding profile as the monoclonal antibody 3G4 (ATCC PTA 4545); wherein the phospholipid binding profile of the monoclonal antibody 3G4 (ATCC PTA 4545), as determined by relative strength of reactivity in an ELISA, is PS=PA=PI=PG=CL>>PE, wherein > indicates at least 2-fold difference in phospholipid binding and >> indicates at least 10-fold difference in phospholipid binding, each at identical antibody concentrations~~ a

heavy chain variable region that comprises variable heavy (VH) CDR1, VH CDR2 and VH CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said VH CDR1 has the amino acid sequence of SEQ ID NO:10, said VH CDR2 has the amino acid sequence of SEQ ID NO:11 and said VH CDR3 has the amino acid sequence of SEQ ID NO:12; or

(b) ~~an affinity for phosphatidylserine of at least equal to the affinity of the monoclonal antibody 3G4 (ATCC PTA 4545) for phosphatidylserine; wherein the affinity of the monoclonal antibody 3G4 (ATCC PTA 4545) for phosphatidylserine, as determined in said ELISA, has an EC_{50} value of 0.040 µg/ml;~~ a light chain variable region that comprises a variable light (VL) CDR1, VL CDR2 and VL CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said VL CDR1 has the amino acid sequence of SEQ ID NO:13, said VL CDR2 has the amino acid sequence of SEQ ID NO:14 and said VL CDR3 has the amino acid sequence of SEQ ID NO:15

~~and wherein said ELISA comprises:~~

~~(i) adding phosphatidylserine to a solid support;~~

~~(ii) blocking with a blocking buffer comprising 10% serum;~~

~~(iii) adding a primary antibody diluted in said blocking buffer, wherein said primary antibody is said antibody or antigen binding fragment thereof, that binds to phosphatidylserine; and~~

~~(iv) detecting bound primary antibody using a secondary antibody that binds to said primary antibody~~.

99. (Currently Amended) A method for preparing an antibody ~~as defined in claim 97~~, comprising immunizing an animal with activated endothelial cells and selecting from the immunized animal an antibody ~~as defined in claim 97~~ that comprises two variable regions that each comprises three CDRs, wherein at least one of said variable regions is:

(a) a heavy chain variable region that comprises variable heavy (VH) CDR1, VH CDR2 and VH CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said VH CDR1 has the amino acid sequence of SEQ ID NO:10, said VH CDR2 has the amino acid sequence of SEQ ID NO:11 and said VH CDR3 has the amino acid sequence of SEQ ID NO:12; or

(b) a light chain variable region that comprises a variable light (VL) CDR1, VL CDR2 and VL CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said VL CDR1 has the amino acid sequence of SEQ ID NO:13, said VL CDR2 has the amino acid sequence of SEQ ID NO:14 and said VL CDR3 has the amino acid sequence of SEQ ID NO:15.

Claims 100-105 canceled

106. (Previously Presented) A composition comprising purified monoclonal antibody 3G4 produced by hybridoma ATCC PTA 4545.

107. (Currently Amended) A composition comprising a first purified antibody, ~~wherein a human antibody framework or constant region is operatively attached to an~~ or antigen-binding region ~~of an antibody that binds to phosphatidylserine and effectively competes with the~~

~~monoclonal antibody 3G4 (ATCC PTA 4545) for binding to phosphatidylserine in an ELISA that comprises~~ thereof, and at least a second therapeutic agent; wherein said first antibody or antigen-binding region thereof comprises at least two variable regions that each comprises three CDRs, wherein said two variable regions are:

(a) ~~adding phosphatidylserine to a solid support;~~ a heavy chain variable region that comprises a variable heavy (VH) CDR1, VH CDR2 and VH CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said variable heavy (VH) CDR1 has the amino acid sequence of SEQ ID NO:10, said VH CDR2 has the amino acid sequence of SEQ ID NO:11 and said VH CDR3 has the amino acid sequence of SEQ ID NO:12; and

(b) ~~blocking with a blocking buffer comprising 10% serum;~~ a light chain variable region that comprises a variable light (VL) CDR1, VL CDR2 and VL CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said variable light (VL) CDR1 has the amino acid sequence of SEQ ID NO:13, said VL CDR2 has the amino acid sequence of SEQ ID NO:14 and said VL CDR3 has the amino acid sequence of SEQ ID NO:15

~~(c) adding a primary antibody diluted in said blocking buffer, wherein said primary antibody is said antibody or antigen-binding fragment thereof, that binds to phosphatidylserine; and~~

~~(d) detecting bound primary antibody using a secondary antibody that binds to said primary antibody~~.

Claims 108-111 canceled

112. (Previously Presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a biologically effective amount of purified monoclonal antibody 3G4 produced by hybridoma ATCC PTA 4545.

Claims 113-116 canceled

117. (Previously Presented) Purified monoclonal antibody 3G4 produced by hybridoma ATCC PTA 4545.

Claims 118-121 canceled

122. (Previously Presented) Hybridoma ATCC PTA 4545.

123. (New) A composition comprising purified monoclonal antibody 3G4 produced by hybridoma ATCC PTA 4545, or an antigen-binding fragment thereof.

124. (New) The composition of claim 123, wherein said composition comprises said antigen-binding fragment of said monoclonal antibody 3G4 produced by hybridoma ATCC PTA 4545.

125. (New) The composition of claim 124, wherein said antigen-binding fragment of said monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, is operatively attached to a human antibody constant region.

126. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a biologically effective amount of purified monoclonal antibody 3G4 produced by hybridoma ATCC PTA 4545, or an antigen-binding fragment thereof.

127. (New) The pharmaceutical composition of claim 126, wherein said pharmaceutical composition comprises said antigen-binding fragment of said monoclonal antibody 3G4 produced by hybridoma ATCC PTA 4545.

128. (New) The pharmaceutical composition of claim 127, wherein said antigen-binding fragment of said monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, is operatively attached to a human antibody constant region.

129. (New) Purified monoclonal antibody 3G4 produced by hybridoma ATCC PTA 4545, or an antigen-binding fragment thereof.

130. (New) A hybridoma that produces a monoclonal antibody that comprises two variable regions that each comprises three CDRs, wherein said two variable regions are:

(a) a heavy chain variable region that comprises a variable heavy (VH) CDR1, VH CDR2 and VH CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said variable heavy (VH) CDR1 has the amino acid sequence of SEQ ID NO:10, said VH CDR2 has the amino acid

sequence of SEQ ID NO:11 and said VH CDR3 has the amino acid sequence of SEQ ID NO:12; and

(b) a light chain variable region that comprises a variable light (VL) CDR1, VL CDR2 and VL CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said variable light (VL) CDR1 has the amino acid sequence of SEQ ID NO:13, said VL CDR2 has the amino acid sequence of SEQ ID NO:14 and said VL CDR3 has the amino acid sequence of SEQ ID NO:15.

131. (New) A hybridoma that produces a monoclonal antibody that comprises two variable regions that each comprises three CDRs, wherein at least one of said variable regions is:

(a) a heavy chain variable region from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, which has the amino acid sequence of SEQ ID NO:2; or

(b) a light chain variable region from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, which has the amino acid sequence of SEQ ID NO:4.

132. (New) The composition of claim 1, wherein said first antibody or antigen-binding fragment thereof comprises said heavy chain variable region.

133. (New) The composition of claim 1, wherein said first antibody or antigen-binding fragment thereof comprises said light chain variable region.

134. (New) The composition of claim 1, wherein said first antibody or antigen-binding fragment thereof comprises said heavy chain variable region and said light chain variable region.

135. (New) The composition of claim 1, wherein said at least a second therapeutic agent is at least a second anti-cancer agent.

136. (New) The pharmaceutical composition of claim 96, wherein said first antibody or antigen-binding fragment thereof comprises said heavy chain variable region.

137. (New) The pharmaceutical composition of claim 96, wherein said first antibody or antigen-binding fragment thereof comprises said light chain variable region.

138. (New) The pharmaceutical composition of claim 96, wherein said first antibody or antigen-binding fragment thereof comprises said heavy chain variable region and said light chain variable region.

139. (New) The pharmaceutical composition of claim 96, wherein said first antibody is an antigen-binding fragment of an antibody.

140. (New) The pharmaceutical composition of claim 139, wherein said first antibody comprises said antigen-binding region of said antibody operatively attached to a human antibody constant region.

141. (New) The pharmaceutical composition of claim 96, wherein said at least a second therapeutic agent is at least a second anti-cancer agent.

142. (New) The kit of claim 97, wherein said first antibody or antigen-binding fragment thereof comprises said heavy chain variable region.

143. (New) The kit of claim 97, wherein said first antibody or antigen-binding fragment thereof comprises said light chain variable region.

144. (New) The kit of claim 97, wherein said first antibody or antigen-binding fragment thereof comprises said heavy chain variable region and said light chain variable region.

145. (New) The kit of claim 97, wherein said first antibody is an antigen-binding fragment of an antibody.

146. (New) The kit of claim 145, wherein said first antibody comprises said antigen-binding region of said antibody operatively attached to a human antibody constant region.

147. (New) The kit of claim 97, wherein said at least a second therapeutic agent is at least a second anti-cancer agent.

148. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a biologically effective amount of a first purified antibody, or antigen-binding fragment thereof, and at least a second therapeutic agent; wherein said first antibody or antigen-binding fragment thereof comprises at least two variable regions that each comprises three CDRs, wherein said two variable regions are:

(a) a heavy chain variable region that comprises a variable heavy (VH) CDR1, VH CDR2 and VH CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said variable heavy (VH) CDR1 has the amino acid sequence of SEQ ID NO:10, said VH CDR2 has the amino acid sequence of SEQ ID NO:11 and said VH CDR3 has the amino acid sequence of SEQ ID NO:12; and

(b) a light chain variable region that comprises a variable light (VL) CDR1, VL CDR2 and VL CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said variable light (VL) CDR1 has the amino acid sequence of SEQ ID NO:13, said VL CDR2 has the amino acid sequence of SEQ ID NO:14 and said VL CDR3 has the amino acid sequence of SEQ ID NO:15.

149. (New) A kit comprising, in at least a first container, a first purified antibody, or antigen-binding fragment thereof, and at least a second therapeutic agent; wherein said first antibody or antigen-binding fragment thereof comprises at least two variable regions that each comprises three CDRs, wherein said two variable regions are:

(a) a heavy chain variable region that comprises a variable heavy (VH) CDR1, VH CDR2 and VH CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said variable heavy (VH) CDR1 has the amino acid sequence of SEQ ID NO:10, said VH CDR2 has the amino acid sequence of SEQ ID NO:11 and said VH CDR3 has the amino acid sequence of SEQ ID NO:12; and

(b) a light chain variable region that comprises a variable light (VL) CDR1, VL CDR2 and VL CDR3 from the monoclonal antibody 3G4, produced by hybridoma ATCC PTA 4545, wherein said variable light (VL) CDR1 has the amino acid sequence of SEQ ID NO:13, said VL CDR2 has the amino acid sequence of SEQ ID NO:14 and said VL CDR3 has the amino acid sequence of SEQ ID NO:15.